

FIGURE 1

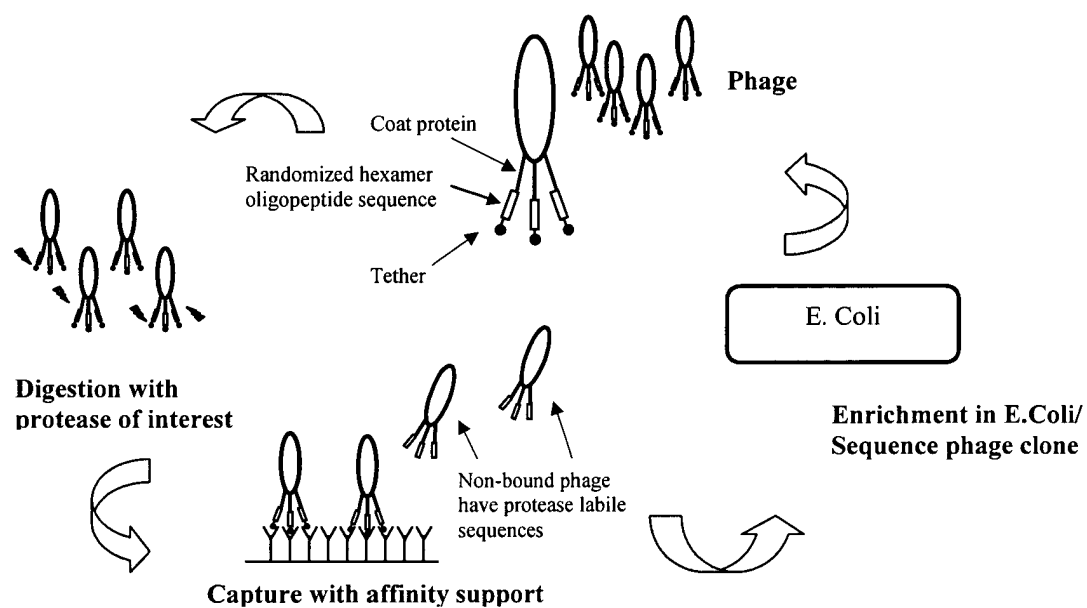


FIGURE 2

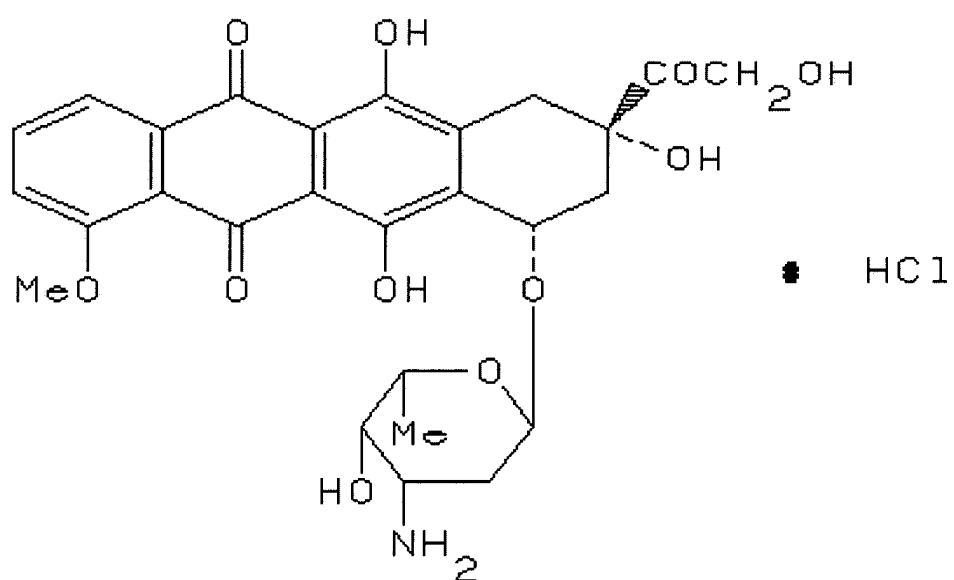
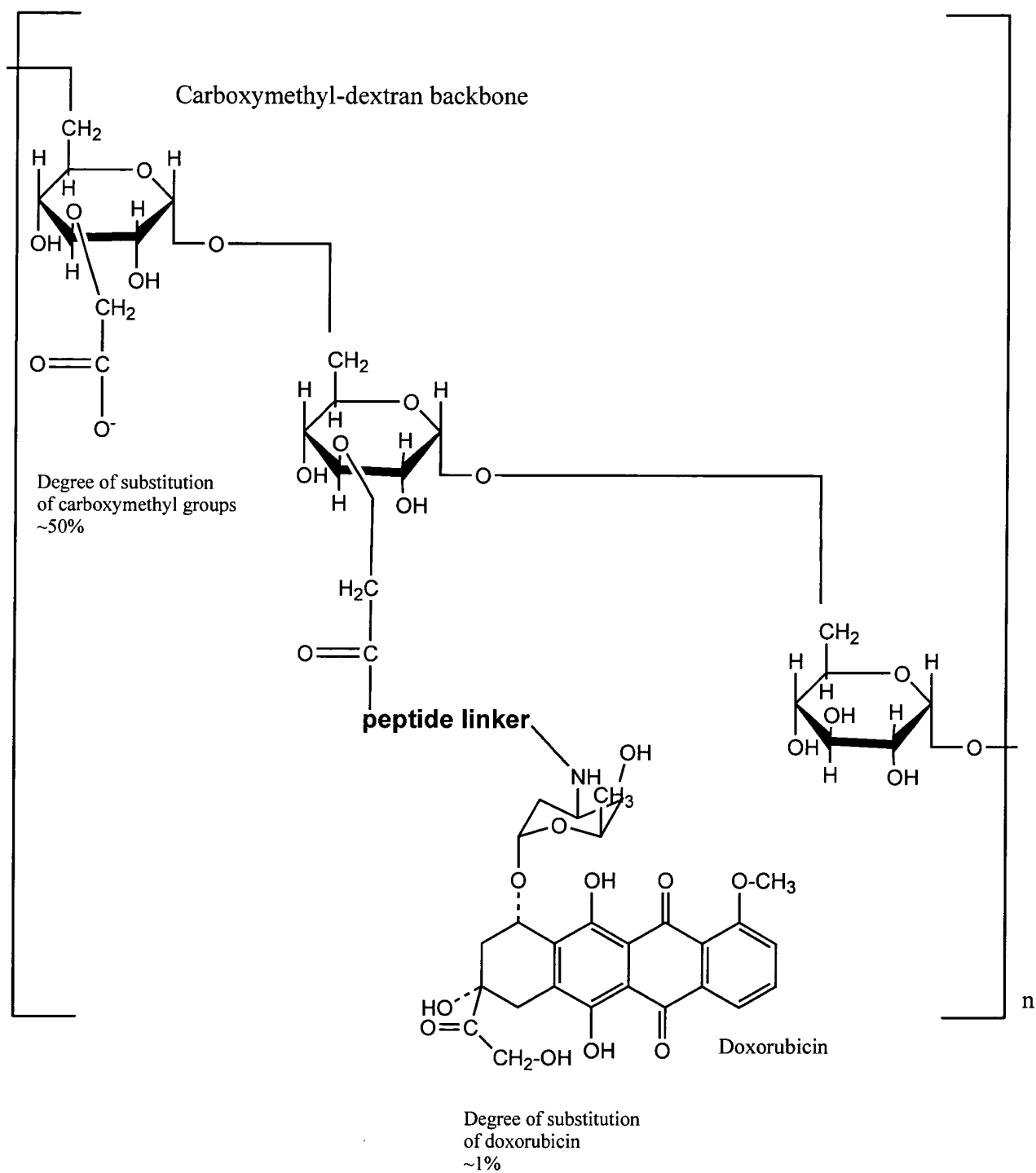


FIGURE 3



**FIGURE 4**

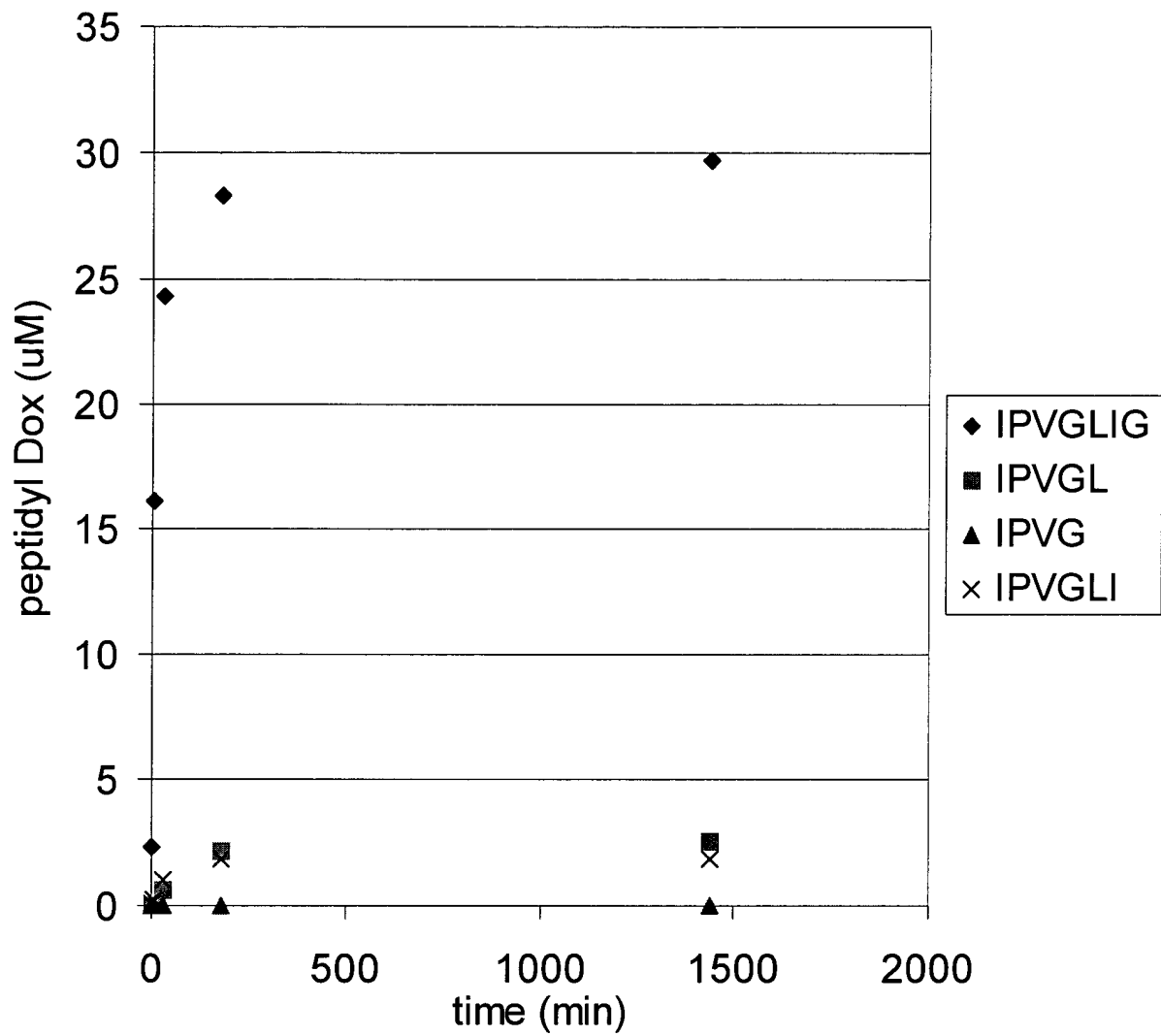


FIGURE 5A

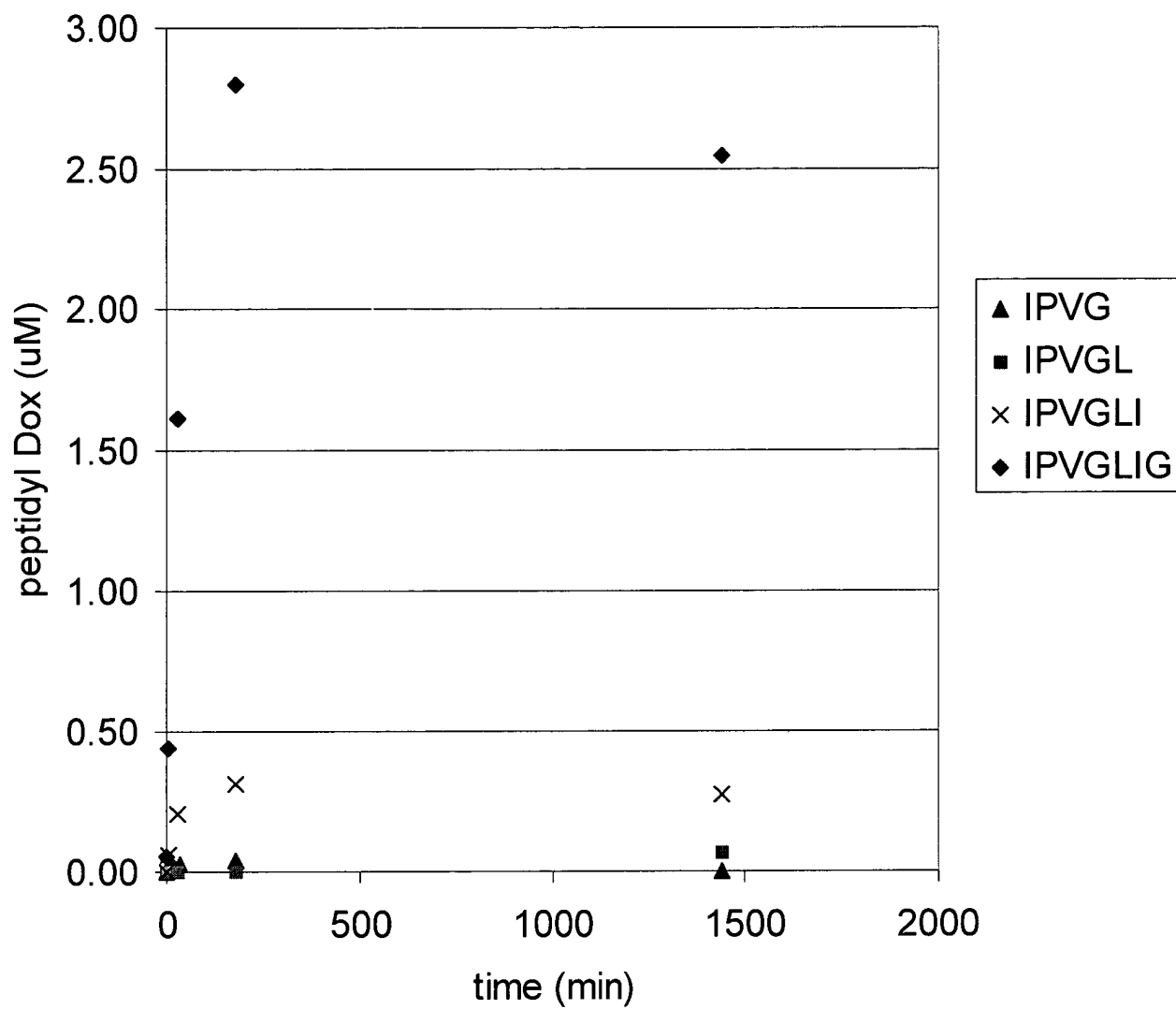


FIGURE 5B

FIGURE 6A (HT-1080)

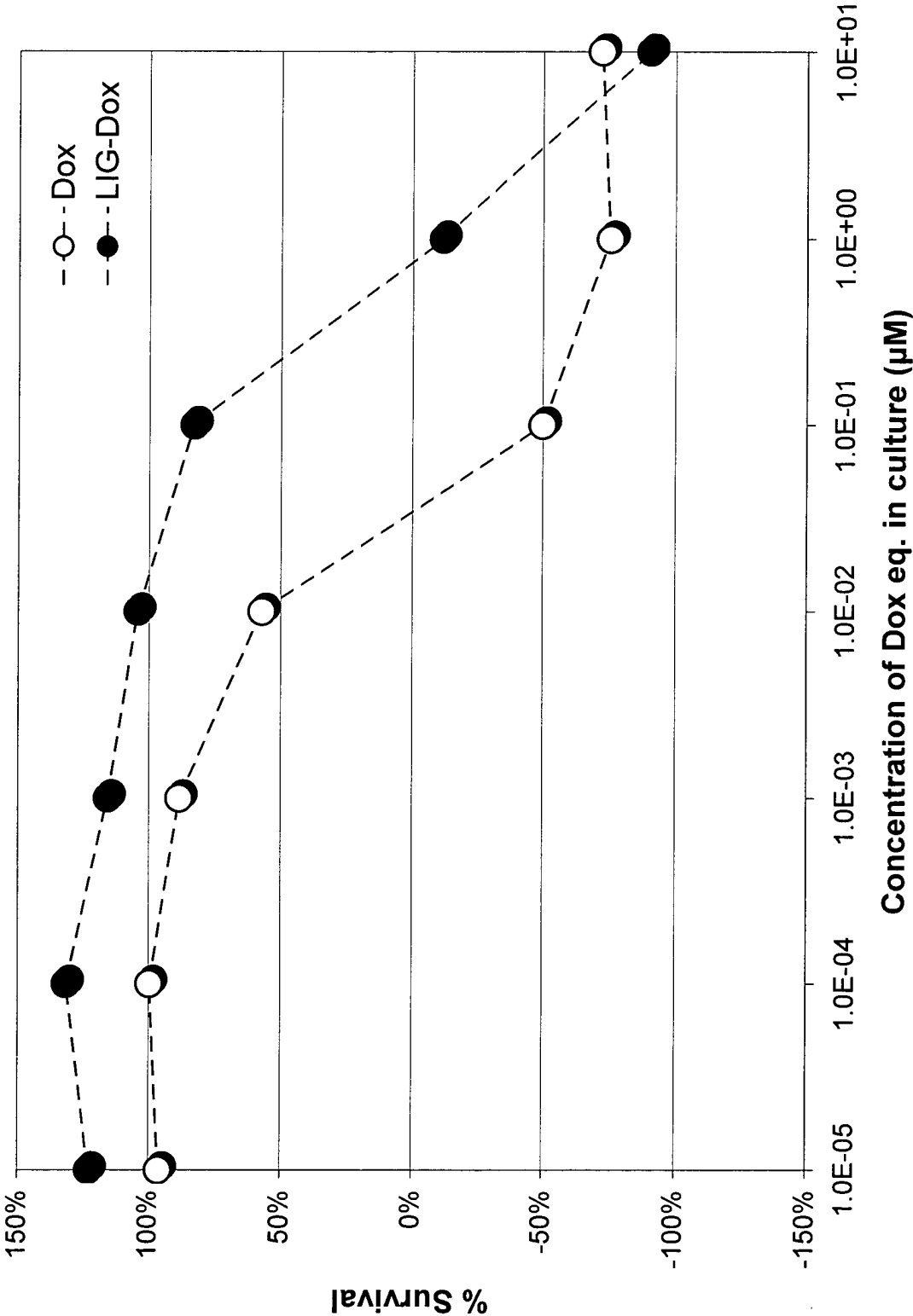


FIGURE 6B (BT-20)

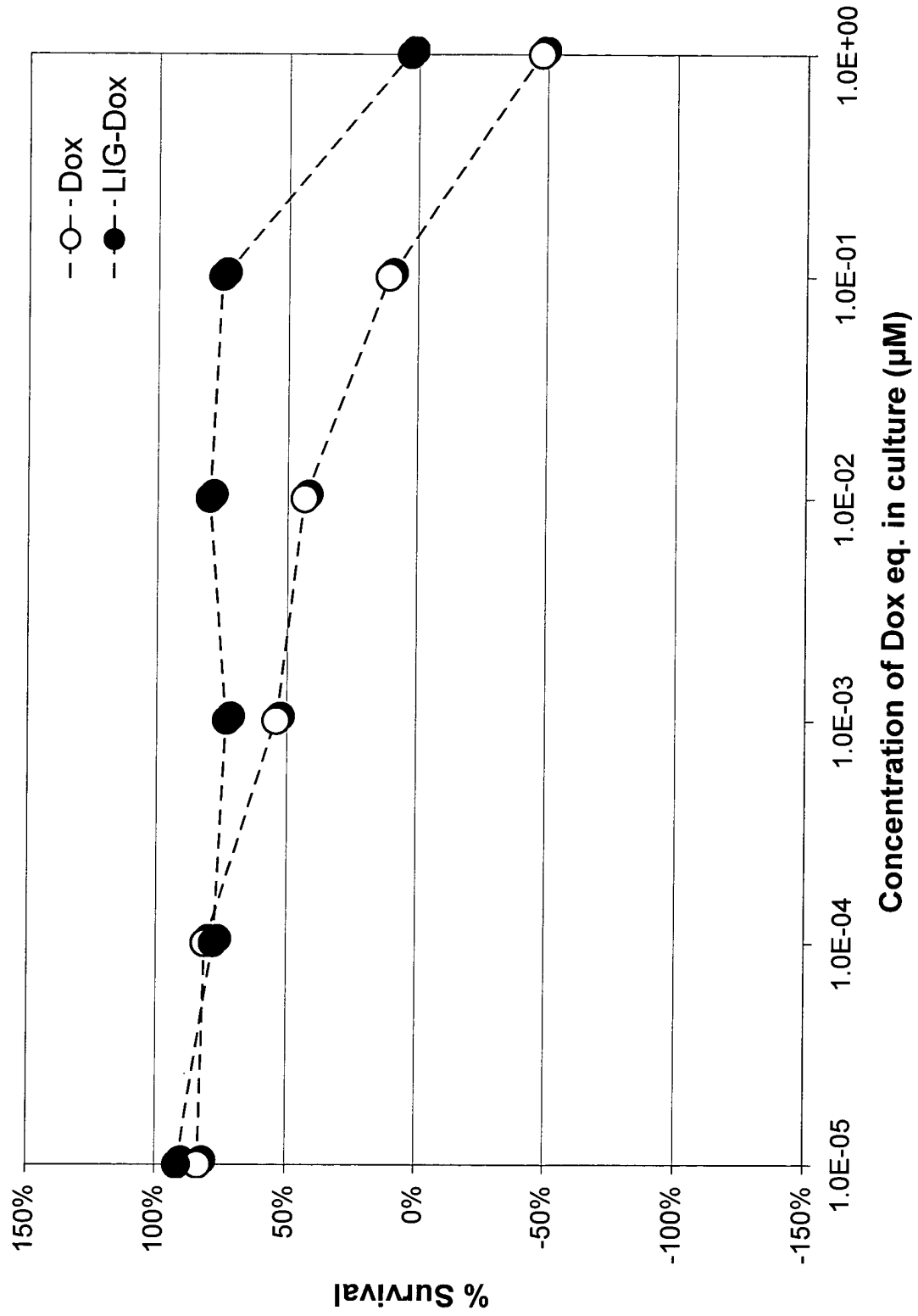




FIGURE 6C (U-87)

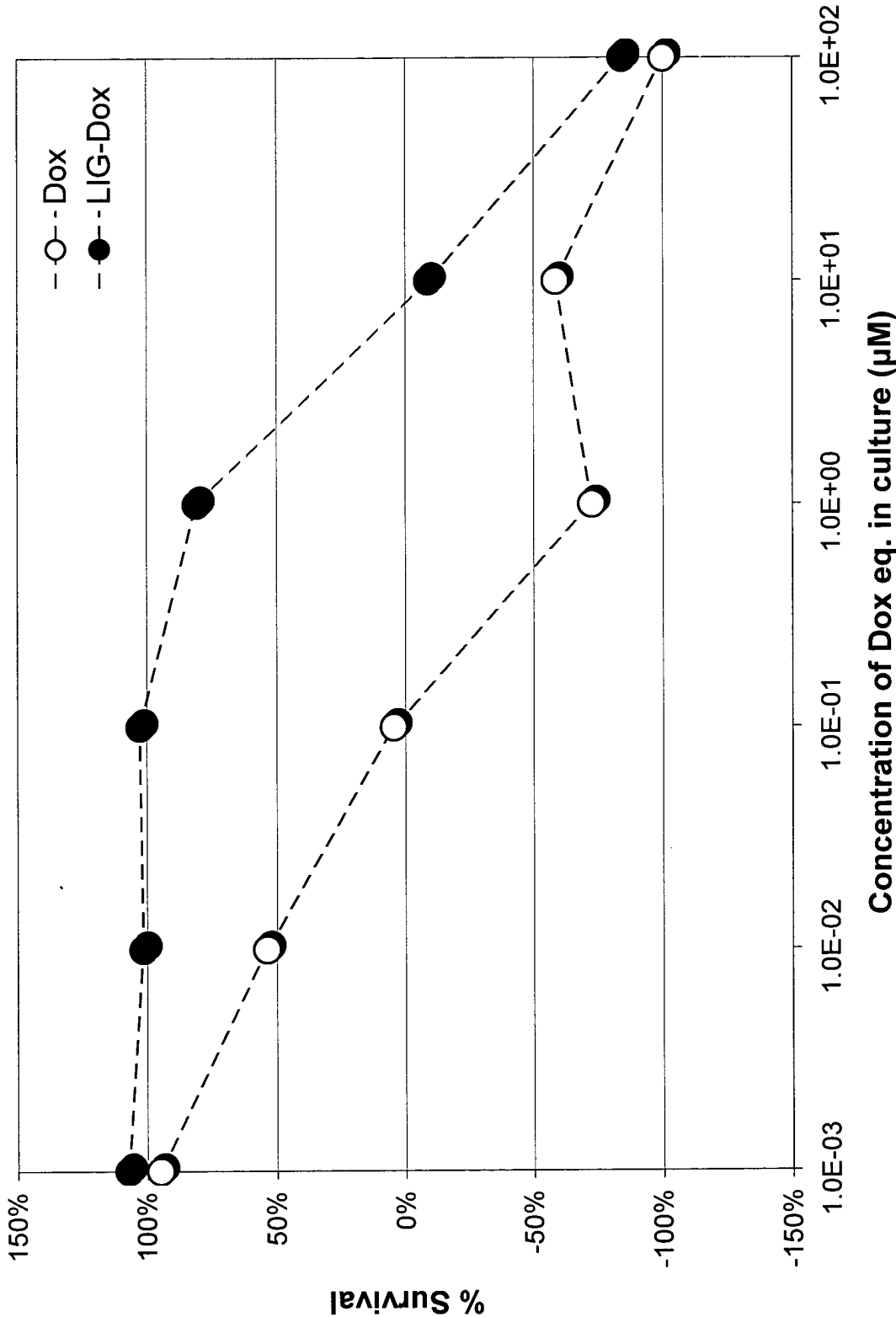


FIGURE 6D (PC-3)

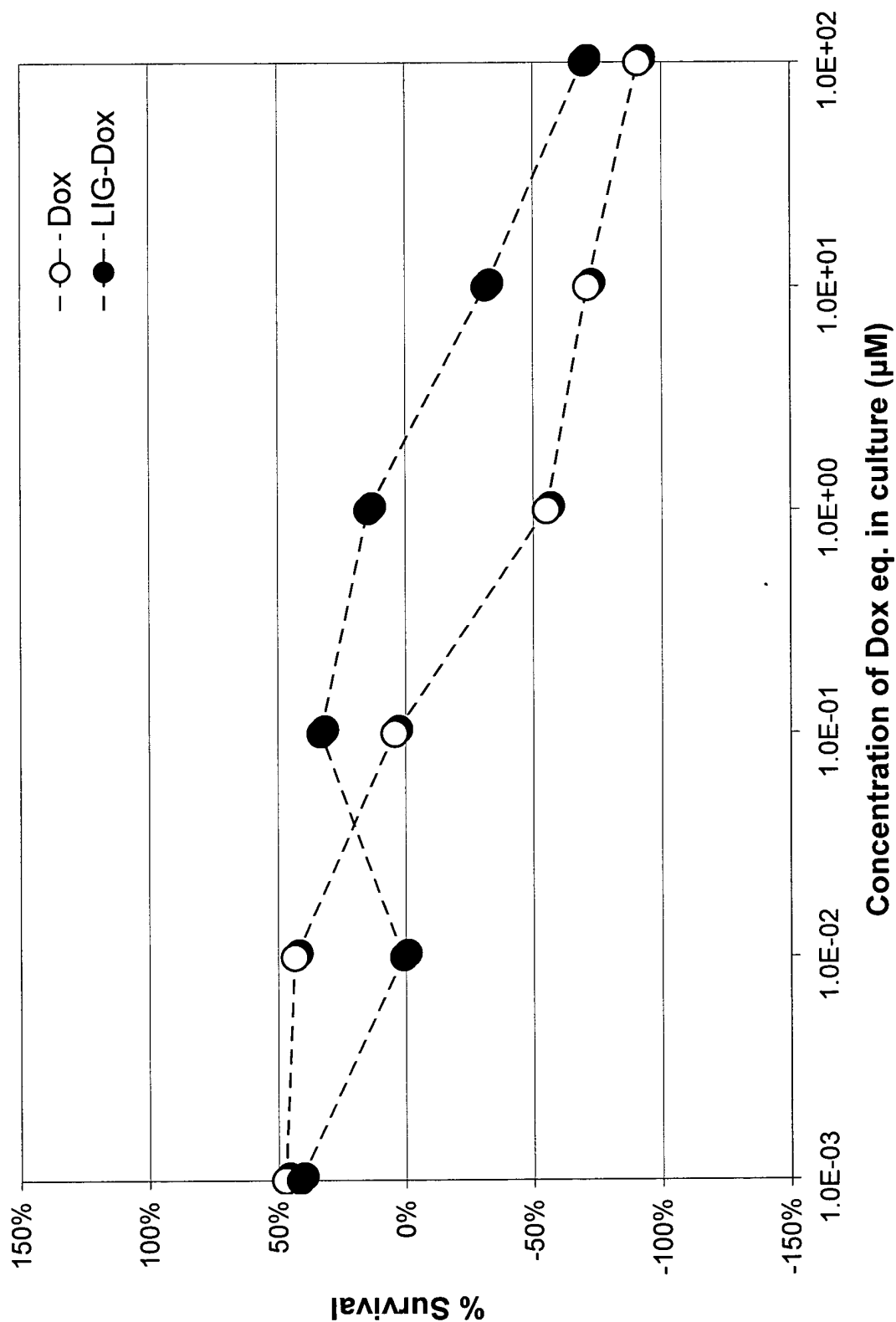


FIGURE 6E (KK-47)

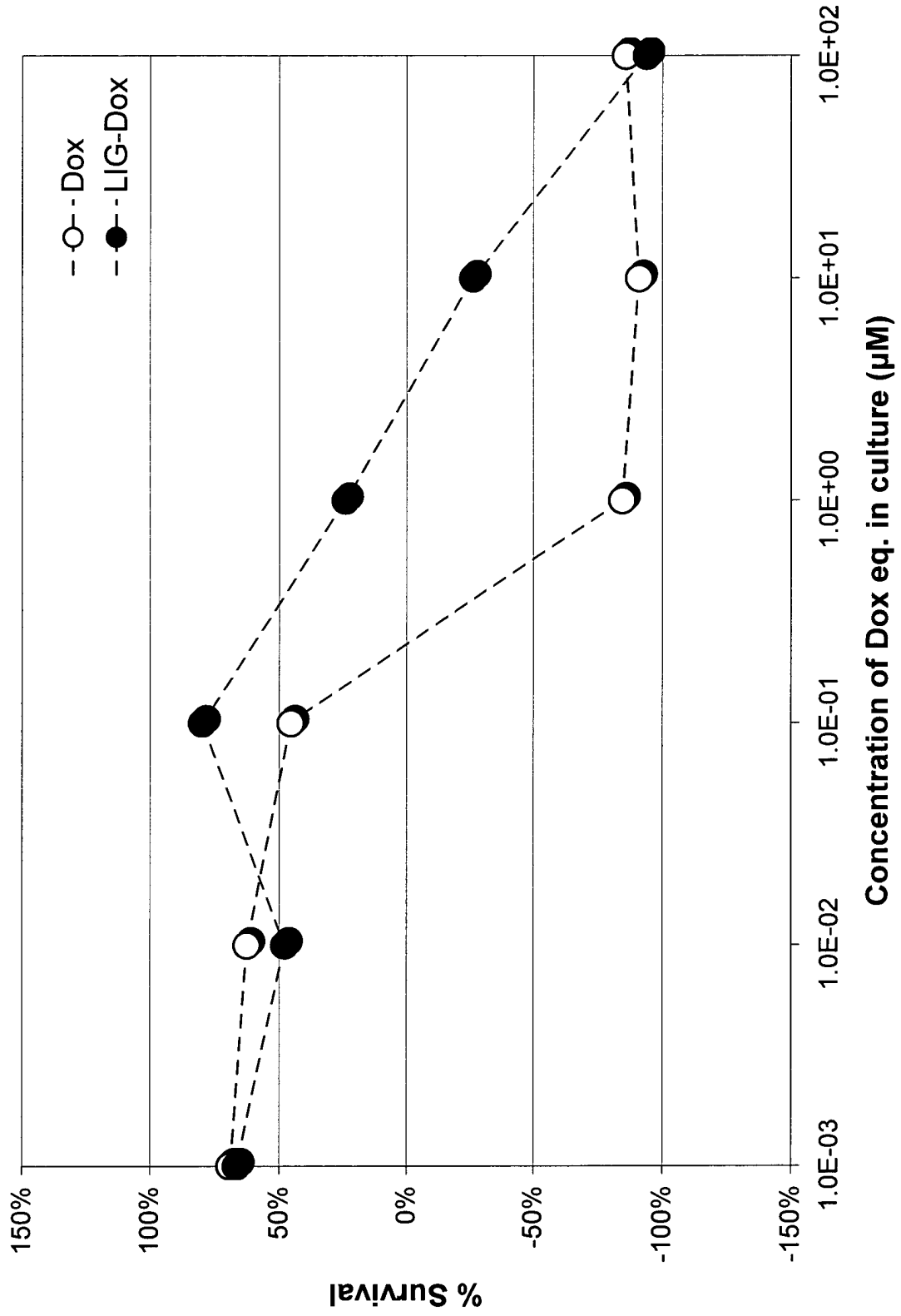
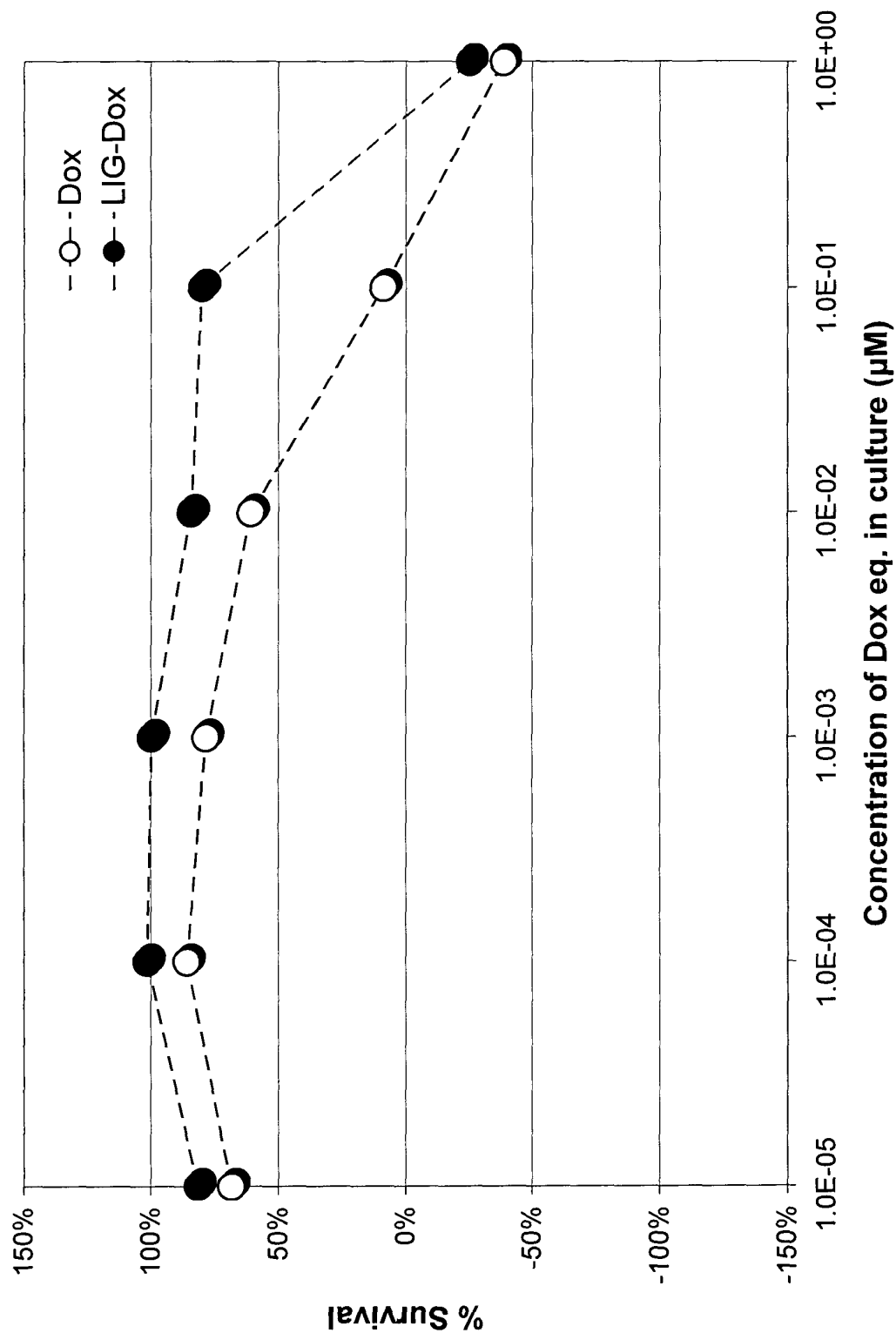


FIGURE 6F (MGH-U1)



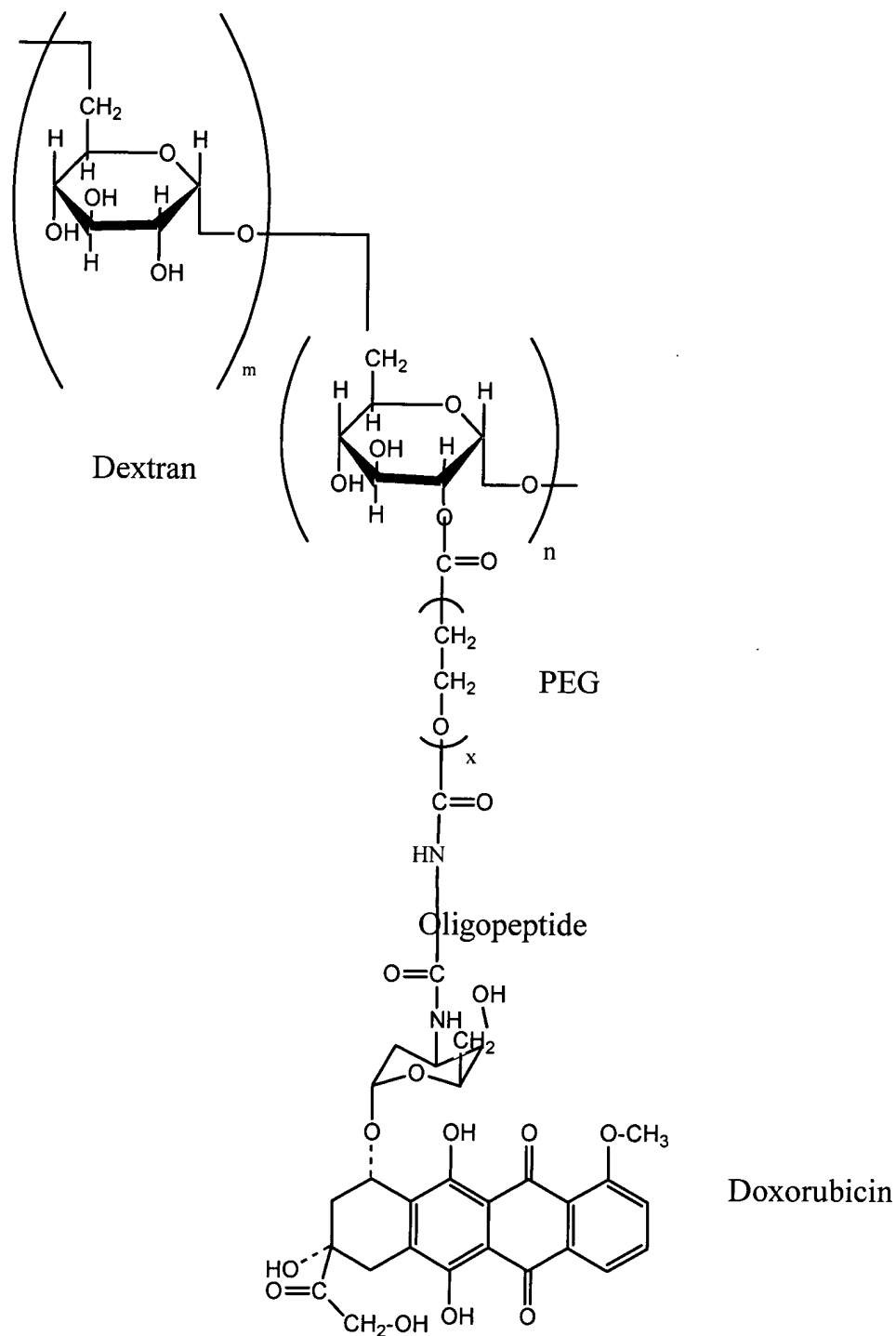


FIGURE 7

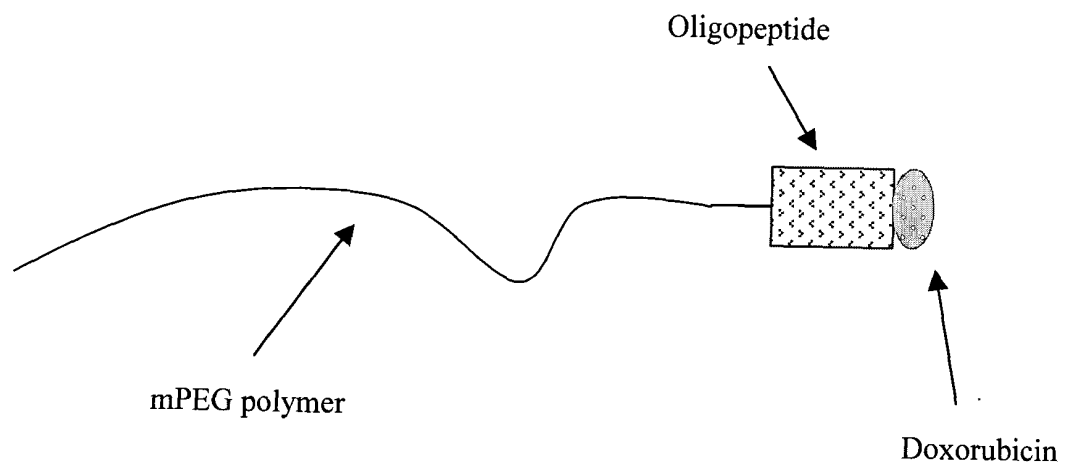


FIGURE 8

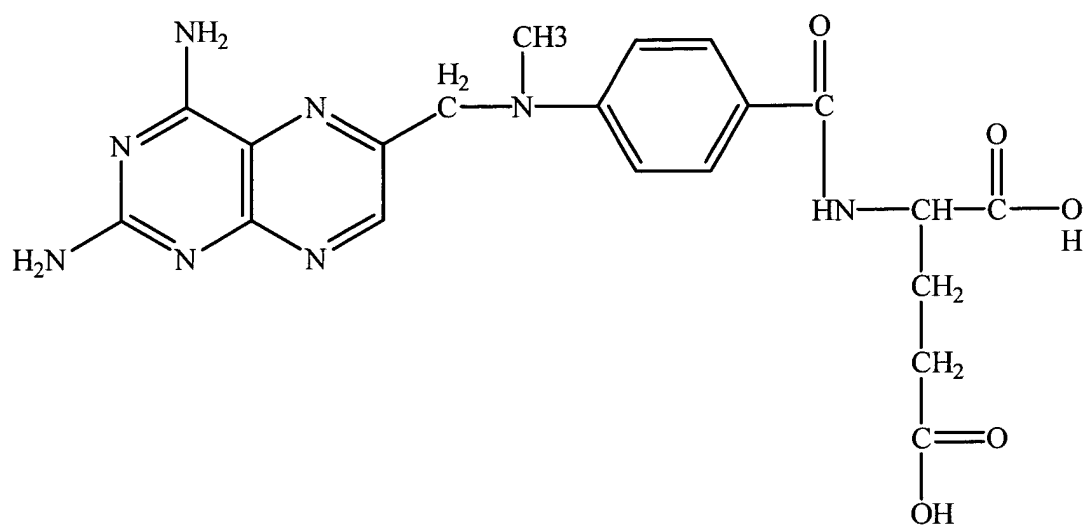


FIGURE 9

FIGURE 10 (HT-1080)

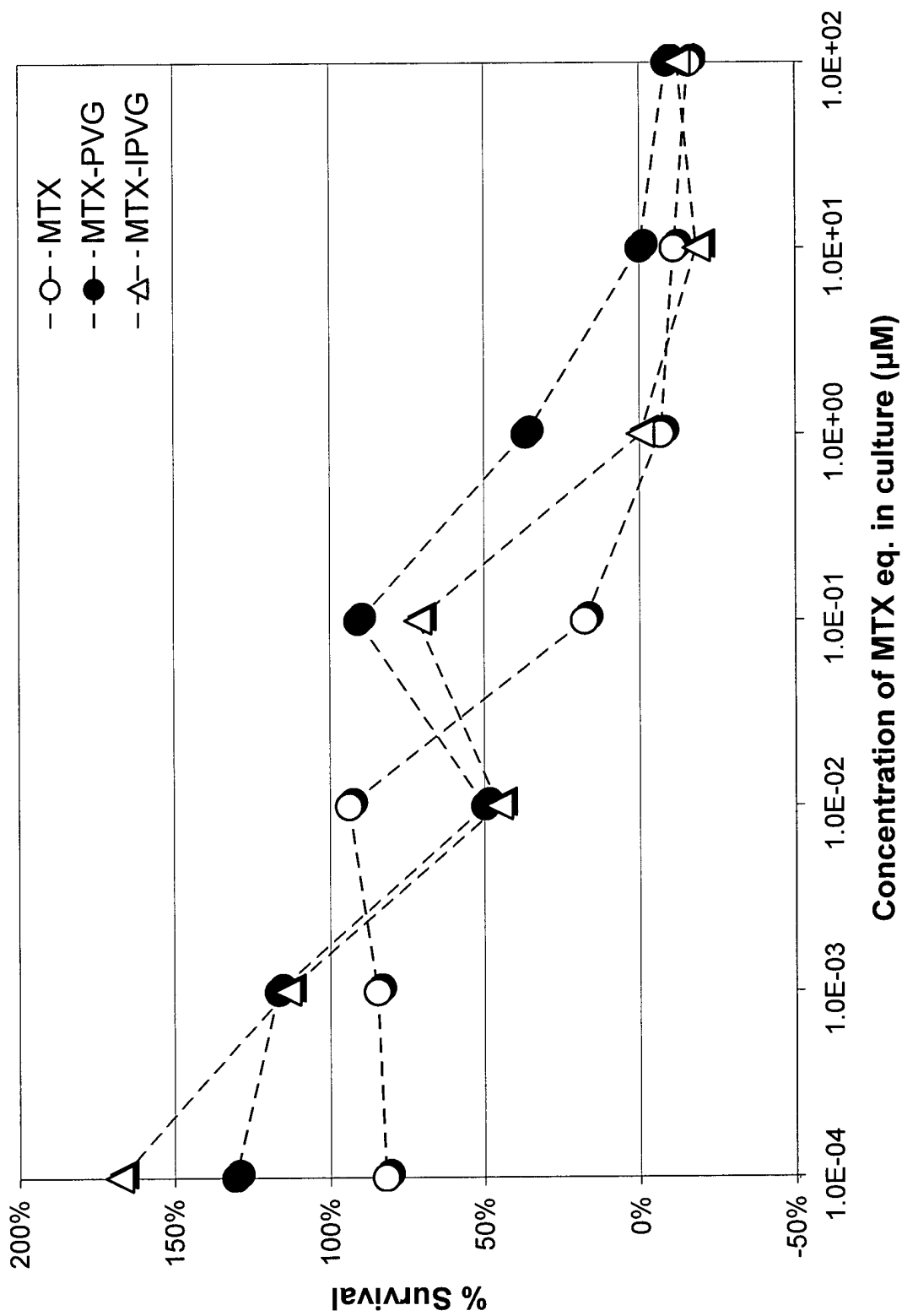




FIGURE 11A (HT-1080)

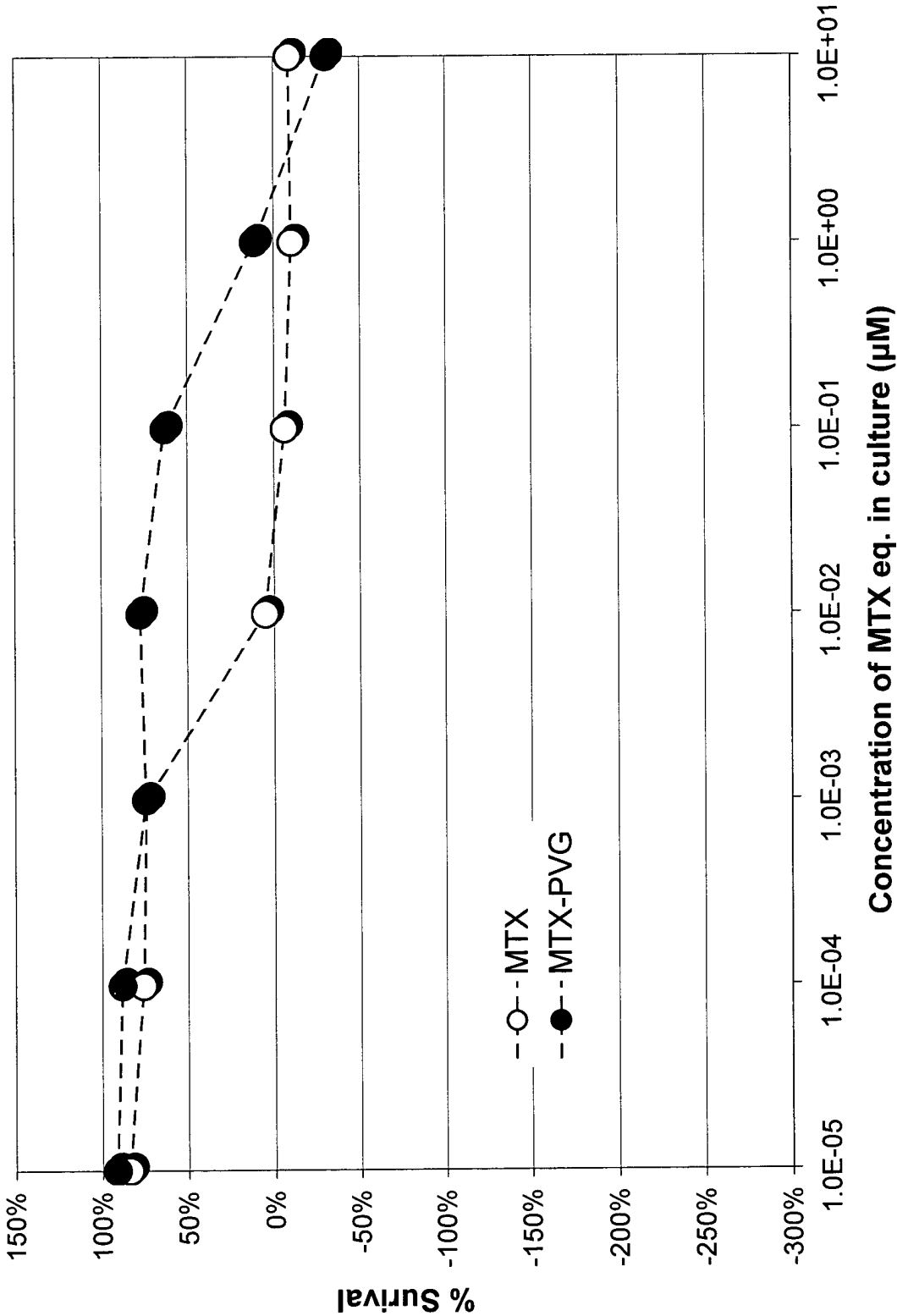


FIGURE 11B (BT-20)

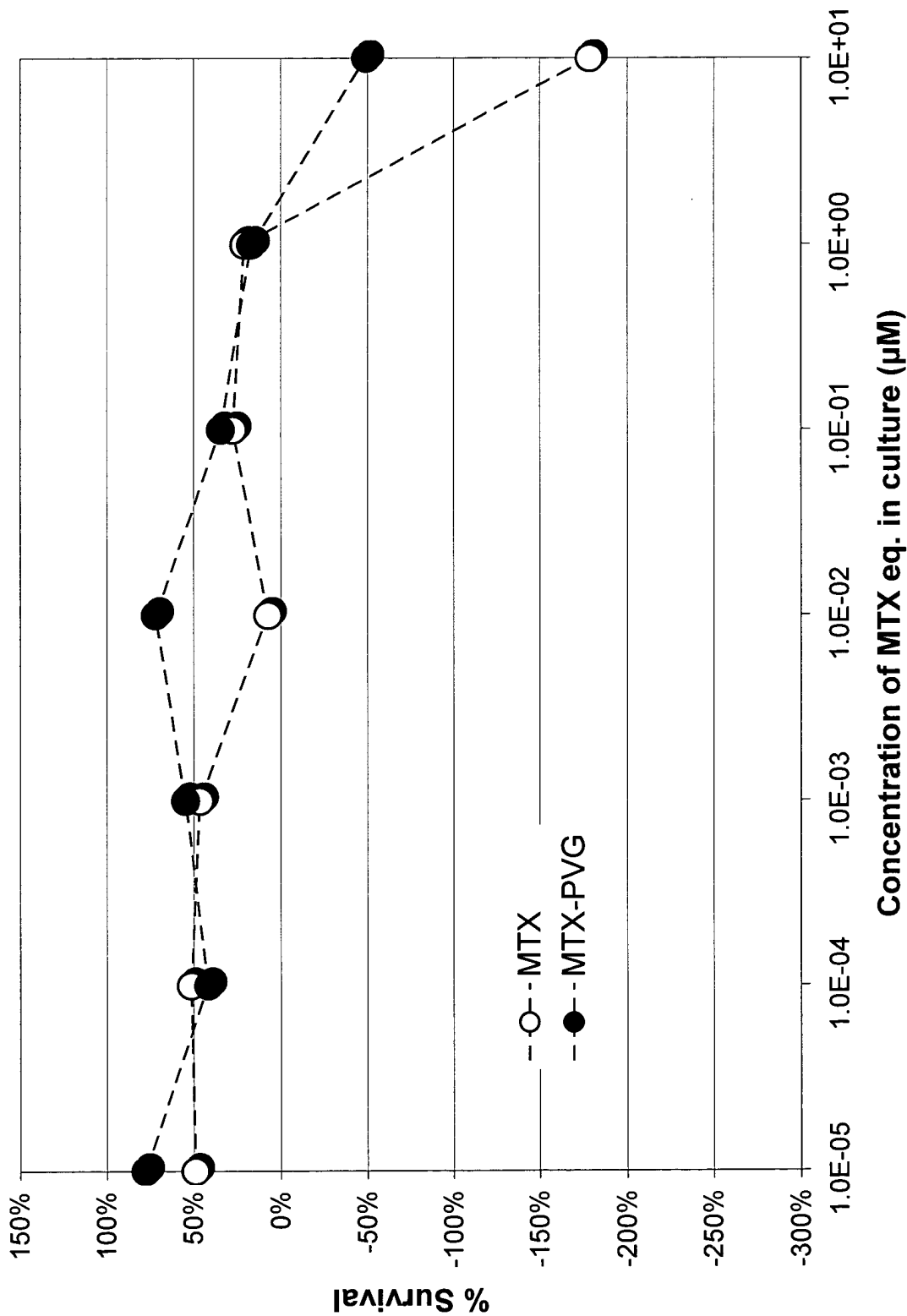
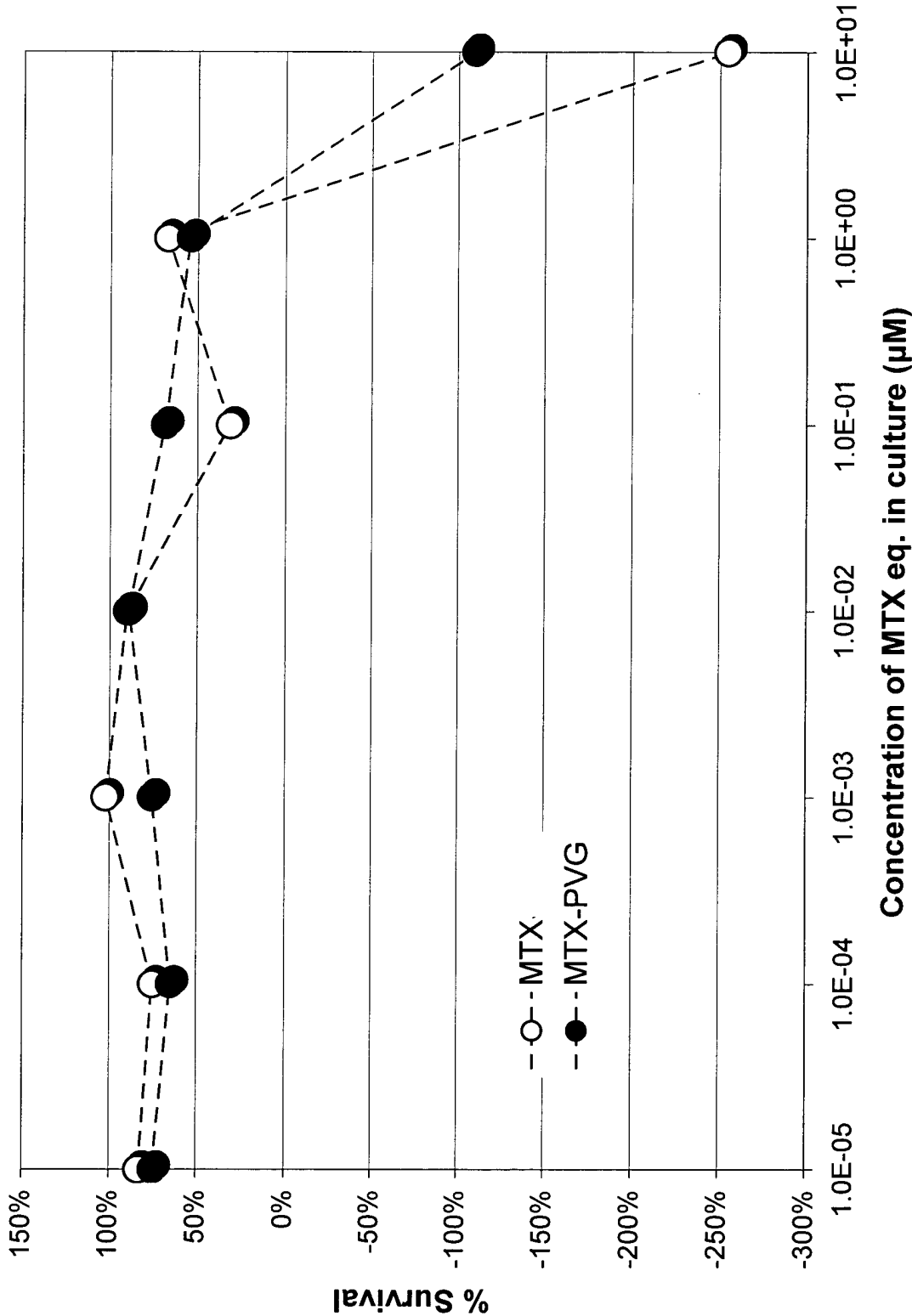
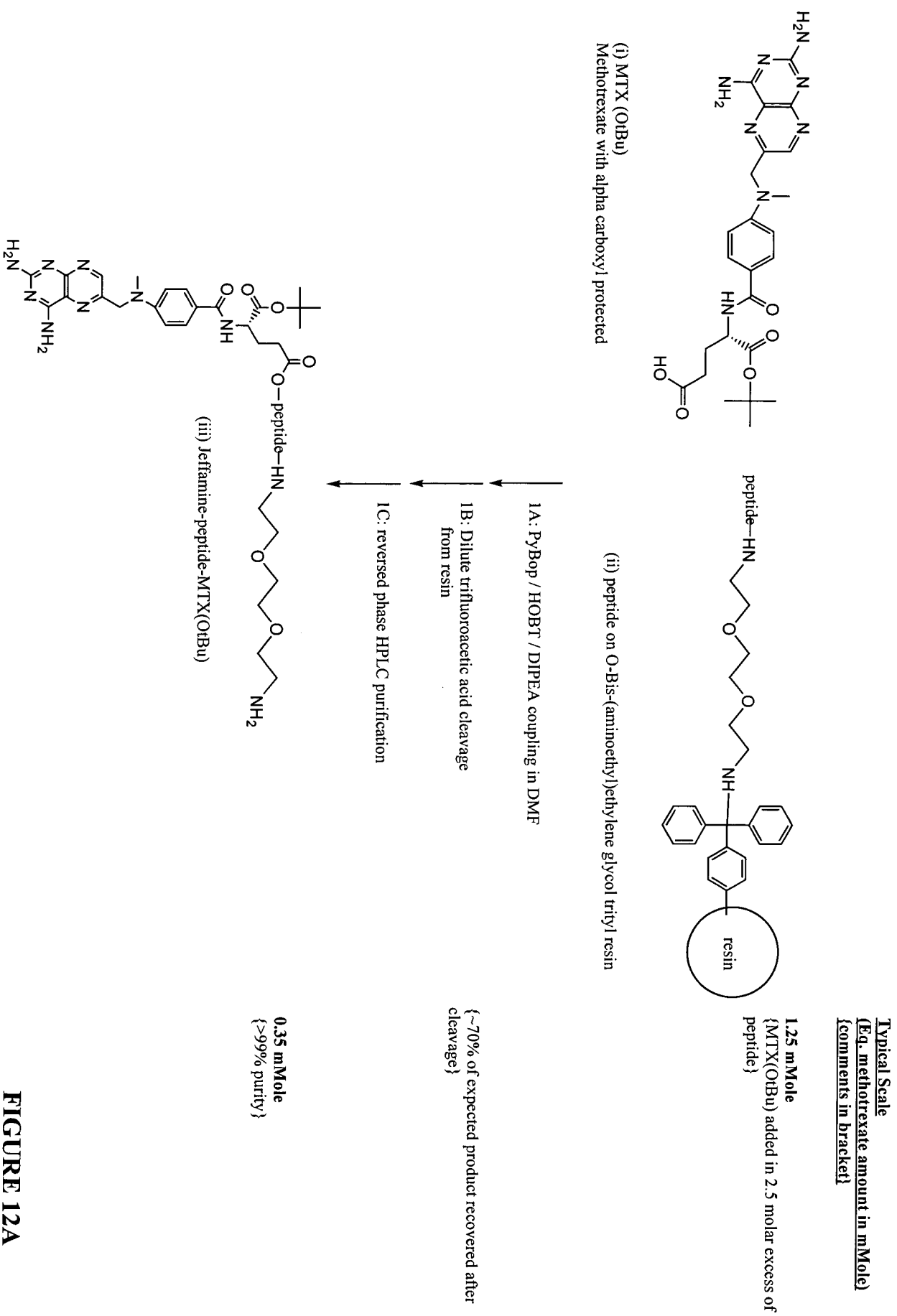


FIGURE 11C (RT-112)





Typical Scale  
 (Eq. methotrexate amount in mMole)  
 {comments in bracket}

0.35 mMole

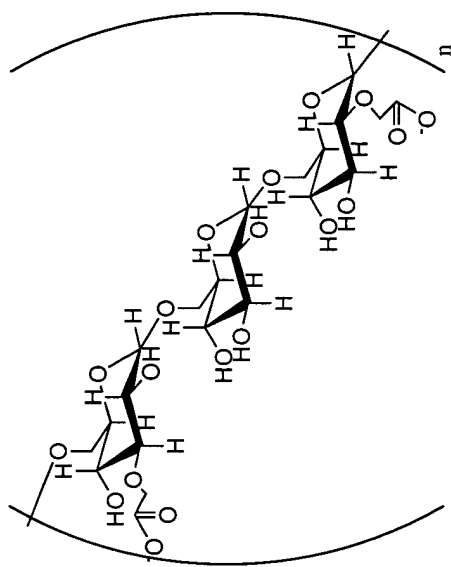
(iv) Carboxymethyl dextran (CM-dextran)  
 degree of substitution of  
 CM groups ~50%  
 nominal MW 70,000

{coupling yield ~ 50%}

{ethanolamine to block remaining  
 carboxymethyl groups}

{step yield ~80%}

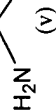
0.14 mMole



2A: coupling with EDC in 0.1M phosphate buffer pH 7.6

2B: charge neutralization by EDC / Ethanolamine in excess

2C: Methanol precipitation



(vi) modified Dextran-peptide-MTX(OTBu)  
 degree of modification ~50%  
 degree of drug loading~1%

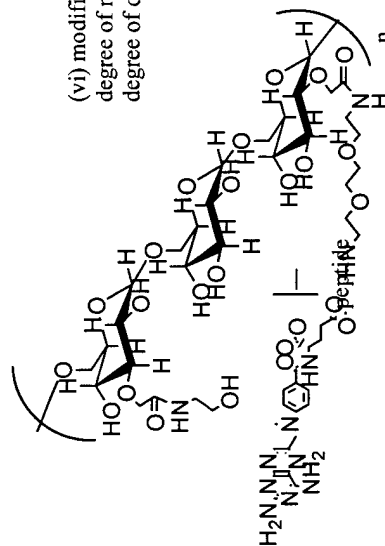
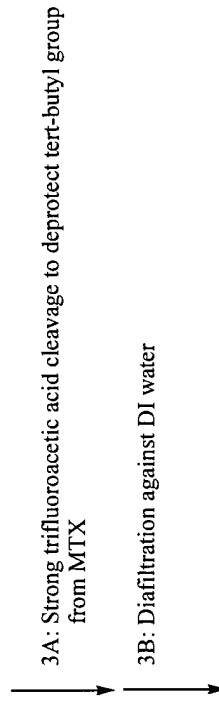
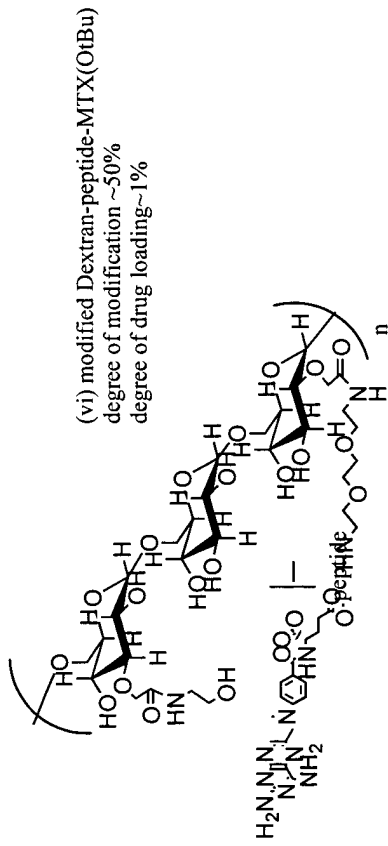


FIGURE 12B

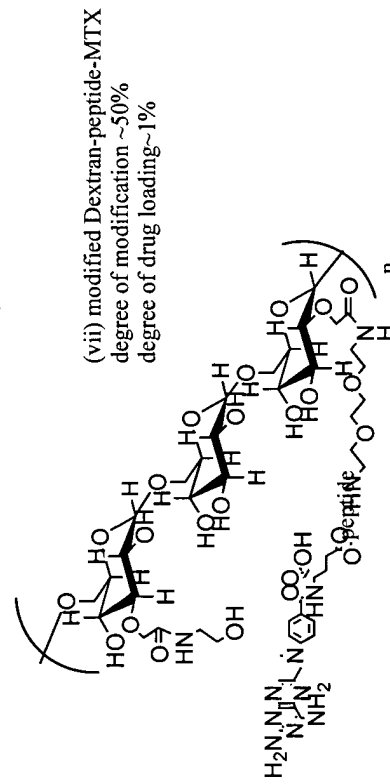
**Typical Scale**  
 (Eq. methotrexate amount in mMole)  
 {comments in bracket}

**0.14mMole**



{step yield ~80%}

**0.11 mMole**



**FIGURE 12C**

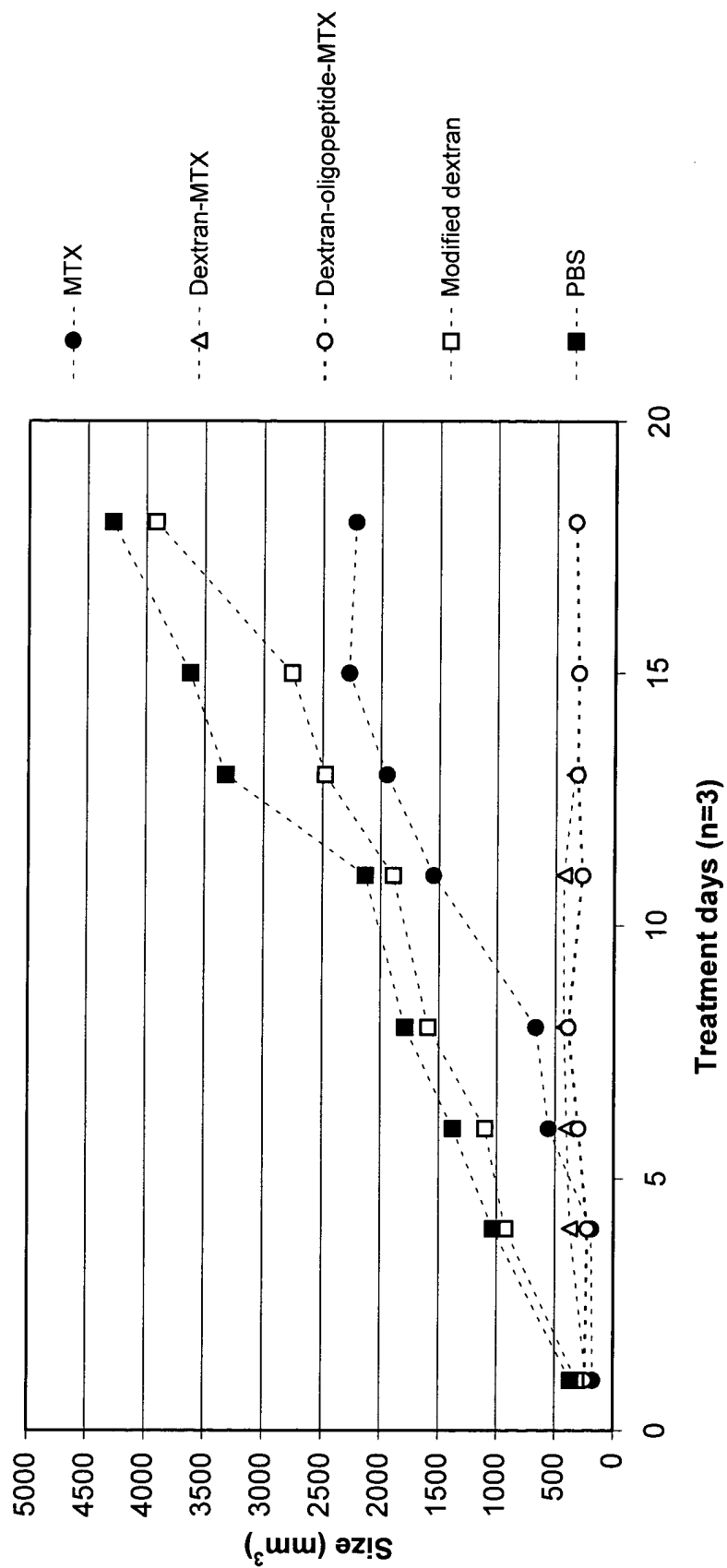


FIGURE 13

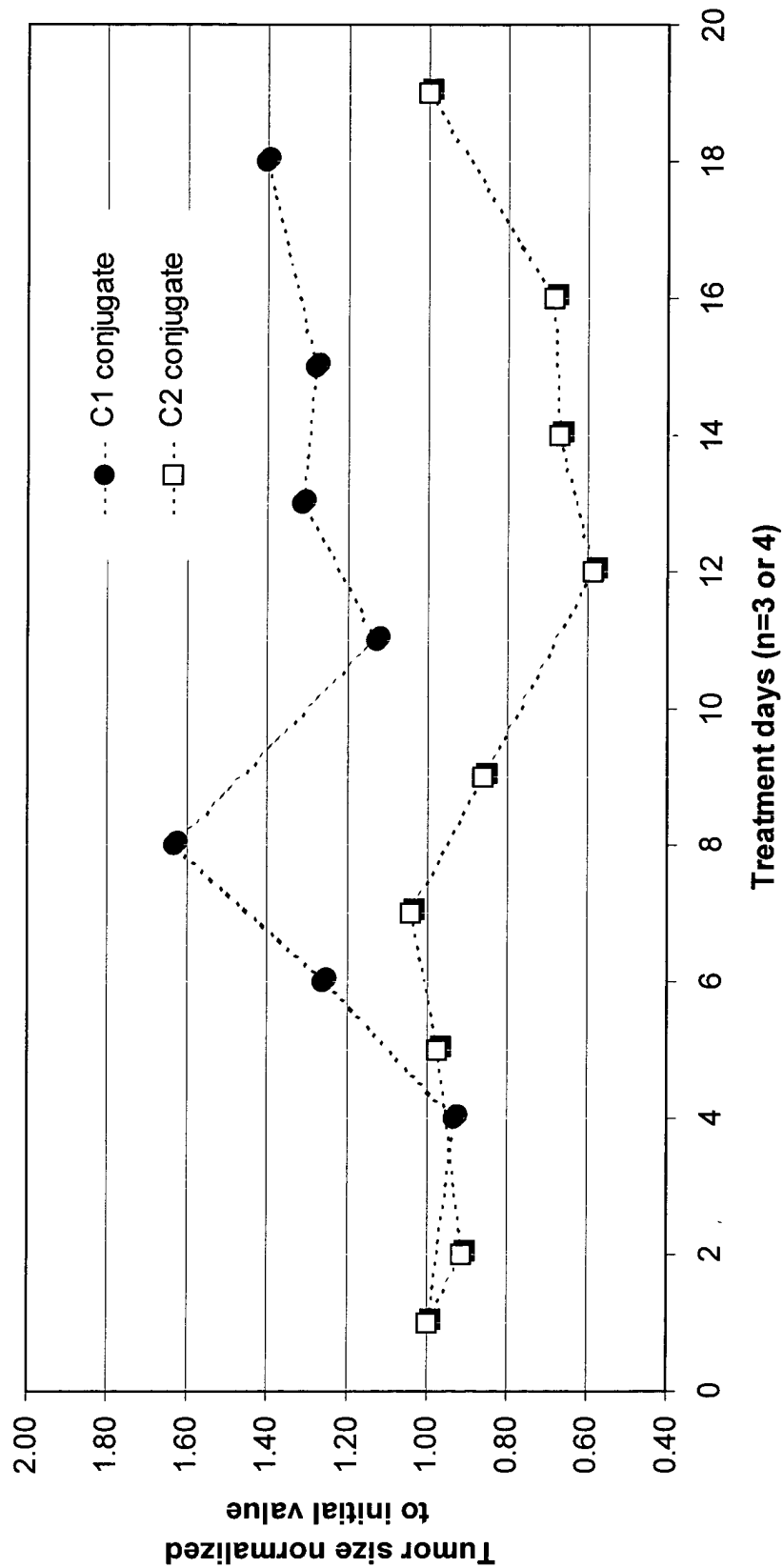


FIGURE 15



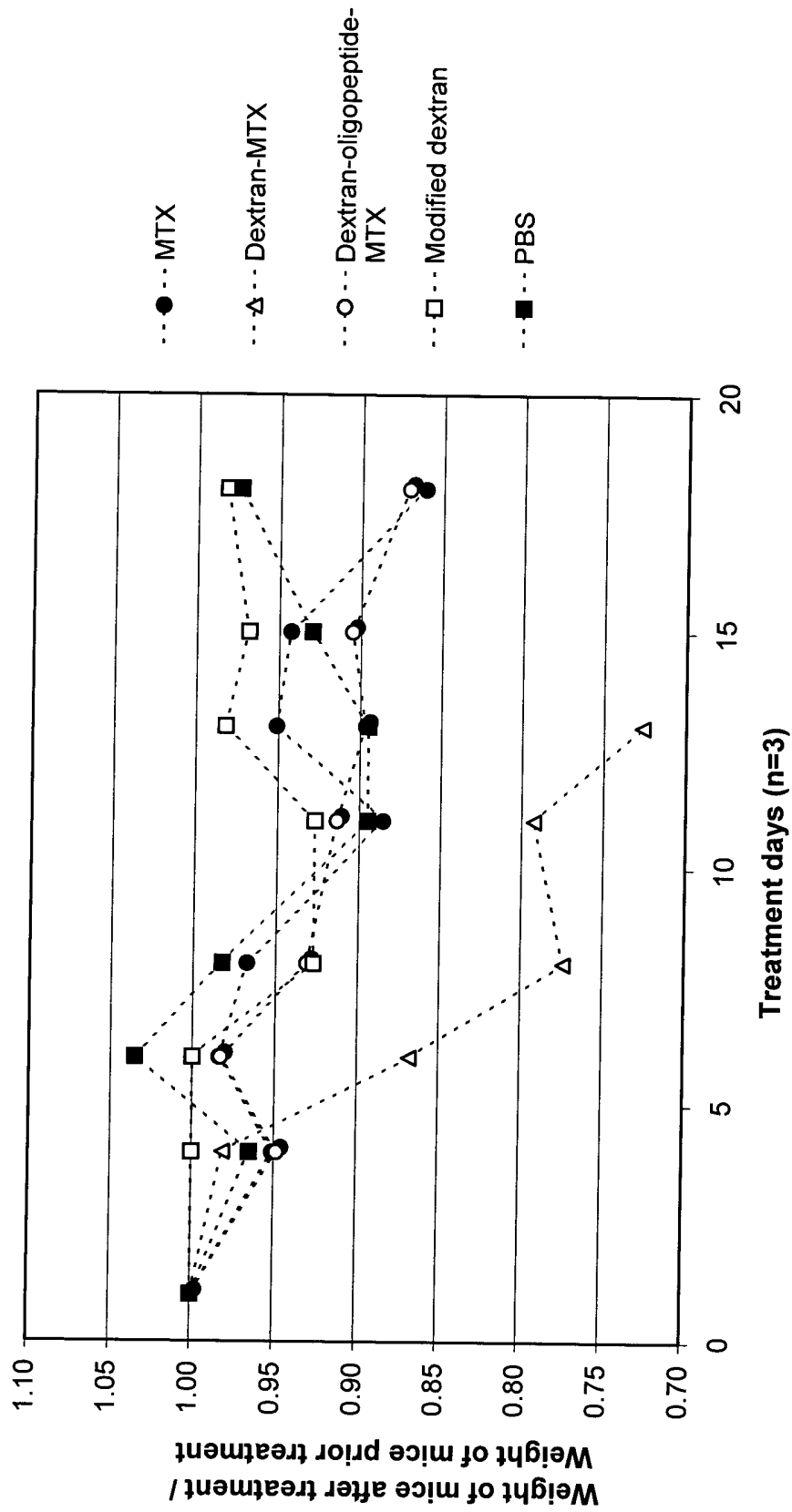


FIGURE 14